OREX.009A

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Gadde et al.
Appl. No.	:	10/440,404
Filed	:	May 19, 2003
For	:	**METHOD FOR TREATING OBESITY**
Examiner	:	Dwayne C. Jones

Group Art Unit 1614

I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: United States Patent and Trademark Office, P.O. Box 2327, Arlington, VA 22202, on

May 17, 2005
(Date)

Sam K. Tahmassebi, Reg. No. 45,151

DECLARATION OF MICHAEL A. COWLEY. SUBMITTED UNDER 37 C.F.R. § 1.132

United States Patent and Trademark Office
P.O. Box 2327
Arlington, VA 22202

Dear Sir:

I, Michael A. Cowley, Ph.D., do hereby declare:

1. I am currently a scientist in the Neuroscience Division at Oregon Health and Science University.

2. I have 6 years of experience studying pharmacological treatments for obesity.

3. The following experiment was carried out by me or under my direct supervision and control.

4. Mice were injected with either saline, bupropion, zonisamide, or a combination of zonisamide and burpropion, and cumulative food intake was measured at various intervals over a 24 hour period. The results, expressed as the proportion of mean food intake by saline-treated mice ± SEM, are given in the table below:

	Hour 1		Hour 2		Hour 4		Hour 8		Hour 24	
	MEAN	SEM(±)	MEAN	SEM(±)	MEAN	SEM(±)	MEAN	SEM(±)	MEAN	SEM(±)
Saline	0.993	0.143	0.996	0.138	0.996	0.130	0.999	0.070	0.999	0.032
Bupropion	0.184	0.079	0.553	0.057	0.994	0.057	1.029	0.061	0.967	0.022
Zonisamide	0.823	0.117	0.812	0.117	1.014	0.111	0.960	0.100	1.005	0.034
Zonisamide + Bupropion	0.534	0.077	0.673	0.086	0.829	0.071	0.875	0.097	0.931	0.052

5. Treatment with bupropion alone initially resulted in a large decrease in food intake in comparison to saline-treated controls (at 1 and 2 hours). However, the effect rapidly attenuated over time so that cumulative food intake in bupropion treated subjects was not significantly different than the intake of saline-treated subjects at 4, 8, or 24 hours after treatment.

6. Treatment with zonisamide alone resulted in a modest decrease in food intake compared to control subjects at the 1 and 2 hour time points, but the effect was fully attenuated at the 4, 8 and 24 hour time points.

7. Treatment with a combination of zonisamide and bupropion resulted in significantly decreased food intake compared to saline-treated control subjects at all time periods measured. These results were unexpected based on results with zonisamide and bupropion alone, since the magnitude of the decrease in subjects treated with the combination was greater at the 4, 8, and 24 hour time points than the additive effects observed for the compounds administered by themselves. Thus, the combination of zonisamide and bupropion had a synergistic effect on food intake, resulting in a significant decrease at the 4, 8 and 24 hour time points where no decrease was observed with either compound administered alone.

8. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful, false statements may jeopardize the validity of the application or patent issuing therefrom.

Respectfully submitted,

Dated: 4-26/05

By: /Michael Cowley/
Michael A. Cowley, Ph.D.

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